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The role of conservative treatment in morbid obesity (minireview)

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The article analyzes the treatment of long-term weight increment, morbid obesity and non-alcoholic steatohepatosis of the liver through medication, diet, lifestyle changes, and physical activity. An analysis of the literary data suggests that at morbid obesity, lifestyle changes, increased physical activity, different diets, or medications do not provide a basis for complete cure of the disease. After stopping taking both drugs and cures to reduce body weight, it begins to increase again.

Keywords: *Body weight, morbid obesity, diet, drug treatment*

Obesity and type-2 diabetes are interrelated and are considered to be the epidemic of the XXI century. Approximately ¼ part of the population in economically developed countries suffers from this disease. According to the World Health Organization, by 2025, 2.3 of the world's elderly overweight and morbidly obese (Jensen et al., 2014; Younossi et al., 2016).

Visceral obesity plays an important role in the development of insulin resistance, type-2 diabetes, non-alcoholic steatohepatosis of the liver, cardiovascular diseases. Therefore, the treatment of this disease is in the focus of attention of the medical community, both in the past and in the present century.

Many researchers are devoting their research to developing different methods to prolong the lives of those with the disease, and are working to prevent the association of morbid obesity with other diseases and to improve the quality of life and psychological status of patients. Decreasing of the body weight, blood sugar and blood pressure were considered as the main criteria for treatment.

Recently, some changes have been made in the main criteria for the treatment of morbid obesity. If in the past the attending physician tried to reduce body weight suddenly, now it is recommended to perform this procedure gradually. L.V.Savelieva shows that the gradual reduction of body weight (0.5-1.0 kg per week) in patients with morbid obesity, as well as non-alcoholic fatty liver is more effective in terms of compensation of metabolic syndrome (Savelieva, 2011**)**.

S.A.Buturova considers that if treatment reduces body weight by 10% before treatment, it should be considered an effective treatment (Buturova 2004).

From the first years of the XXI century, doctors have tried to treat this disease with medication, lifestyle changes and various diets (Promrat et al., 2010; Marra et al., 2013; Eckard et al., 2013). Thanks to research in this area, a new strategy for morbid obesity, as well as non-alcoholic obesity of the liver has been developed. According to this strategy, treatment consists of gradually reducing body weight by changing lifestyle. For this purpose, the treatment period is divided into the following stages:

1. The period of weight loss - 3-6 months;
2. Stabilization of body weight - 6-12 months:

Malnutrition in the pathogenesis of morbid obesity has led researchers to use diets to treat it. In this regard, diet has been widely used in the treatment of morbid obesity since the end of the last century, including the first decade of modern times (Rytting et al., 1995; Astrup, 2000; Lichtenstein, 2006). However, the diet is not based on a single system. Some authors prefer to eliminate high-calorie foods from the diet, while others prefer to limit fats and carbohydrates without compromising total calories.

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L.V.Savelieva took a more realistic approach to dieting (Savelieva, 2011). According to her, before determining the composition of the diet, it is recommended to take into account the patient's diet and what type of food he prefers when eating. According to him, the patient should keep a daily weight record to control his/her weight while eating according to the prescribed diet.

On the basis of this registration, the nutritionist should monitor the changes in the patient's condition and, if necessary, make some changes in the diet.

At present, nutritionists prefer the WHO-approved diet. According to the WHO, in addition to reducing calories from the diet, it is necessary to limit the taking of fats.

Thus, the diet should consist of 10-15% protein, 55-60% carbohydrates, 25-30% fat (provided that the fats of animal origin do not exceed ⅓). When calculating calories, the patient's age, weight, sexual and physical activity should be taken into account. In addition, the diet should be adjusted to the changes in the patient's blood. If excess body weight has caused dyslipidemia in the blood, it is necessary to limit the entry of nutrients and cholesterol into the body to 250-300 g.

Also, the daily intake of salt in the diet of people with high blood pressure should be reduced to 5 grams.

Thus, by the first decade of the 21st century, the increase in diet and physical activity in the treatment of morbid obesity was more widespread.

The authors of this idea (Savelieva, 2011; Popov et al., 2015; Lazebnik et al., 2017; Zhirkov et al., 2019; Wong et al., 2013 etc.) believe that the establishment of this aspect of treatment in patients with morbid obesity and non-alcoholic fatty liver based on it can reduce elevated levels of liver enzymes in the blood without the use of pharmacological drugs is successful. According to their data, the proposed diet has led to a decrease in adipose tissue in the liver and an improvement in the histological structure of the liver.

However, this idea has not been unequivocally accepted in the scientific literature.

Promart et al. believe that the treatment of non-alcoholic liver obesity cannot be achieved by diet alone (Promart et al., 2010). According to them, the diet should be accompanied by a variety of physical activities, including track and field athletics, as well as regular brisk fast movement. Summarizing the results of their clinical observations, they concluded that the combined effect of diet and physical activity, along with a decrease in body weight, improves the histological picture of non-alcoholic steatohepatosis of the liver in 3-5% of cases. However, it is unrealistic for Promart and his colleagues to reach such a conclusion without performing a liver biopsy.

F.Maagkos (2010), V.Heijden et al. (2010) note that a diet combined with increased physical activity improves patients with non-alcoholic hepatic obesity. The authors came to this conclusion based on a positive change in the concentration of markers in the blood of patients, including aminotransferase, which reflect the functional state of the liver.

Although dietary treatment of morbid obesity, as well as non-alcoholic liver obesity has been developed, no standard diet has been developed for the treatment of this disease. Most supporters of diet therapy have limited themselves to the proposal to exclude fructose and trans-fats from the diet (Petta et al., 2013; Simopoulos, 2013).

However, clinical observations and experimental results accumulated over time have shown that non-drug therapy is not an effective treatment for morbid obesity.

E.G.Starostina (2011) rightly points out that a special diet and increased physical activity create certain problems in the treatment of morbid obesity, especially in the quality of life of patients. It is known that dieting of overweight people faces the problem of hunger. In addition to having a psychological effect on a person, starvation also results in a violation of the balance of a number of metabolic processes in the body (Timofeeva et al., 2008; Askerov, 2018).

In addition, as noted by Ye.Q.Starostina (2011), diet used as "Treatment starvation" often leads to fatal arrhythmias. In this regard, new, more convenient methods were sought. As a result of these studies, in addition to diet therapy, physical therapy, physiotherapy and psychotherapy are widely used in modern clinical practice in the treatment of morbid obesity. Barte et al. (Barte et al., 2010) note that the application of these methods significantly reduces body weight, lowers blood pressure, stabilizes blood sugar, relieves metabolic

syndrome. As the functional state of the liver improves, the concentration of markers in the blood decreases, and even in 10-15% of patients, the increased concentration of enzymes falls to normal. However, this positive dynamic is not sustainable. After 1-2 years, body weight begins to increase again, and the positive results obtained change in a negative direction.

In the treatment of morbid obesity, the program developed by L.V.Savelieva (Savelieva, 2011) in 1998 at the Scientific Center of Endocrinology of the Russian Federation (Program of therapeutic training and treatment of obese patients) is more advanced method of diet therapy.

The program contains information for patients to get used to diet therapy and physical training, and shows the rules of their conduct. The program was used by 2,000 patients, and the author of the program analyzed the obtained results and concluded that the patients who were difficult to treat, were patients with morbid obesity caused by eating disorders. They not only struggle to follow the diet, but they also die as a result of a number of dietary complications, especially arrhythmias.

Along with all this, a number of researchers have considered the use of drugs in the treatment of morbid obesity and non-alcoholic obesity of the liver, and extensive research has been conducted in this direction (Popov et al., 2015; Ryan et al., 2010; James et al., 2010).

Drugs used for this purpose are divided into 2 groups:

1. Drugs that reduce the need for food.
2. Drugs that reduce the absorption of nutrients.

Although the first drug to reduce the need for food was synthesized in 1893, each drug synthesized was soon withdrawn due to its side effects. About a century later, in 1980-1990, a drug called “Phen-Phen” was synthesized from Phenteramine and Phenfluramine and began to be widely used in medical practice for a long time (Tishkovskiy et al., 2015).

This drug has a stimulating effect on serotonin metabolism through phenfluramine, sympathetic nerve through phentramine. However, over time, the scientific literature began to collect information about its undesirable effects on the body. These data include changes in the heart's valve apparatus, a sharp rise in blood pressure, an increase in the number of heartbeats above normal, and so on, which also restricted the use of this drug (Michka et al., 2010).

Acompila, manufactured by the French company Sanofi-Aventus in Europe since 2006, has entered medical practice and is considered a pathogenetic drug for morbid obesity. This is because the drug drastically reduces the need for food by selectively inhibiting the type 1 receptors of Cannabinoid. However, this drug, which has been popular among gastroenterologists for only 3 years, has been banned from clinical use due to its undesirable side effects on the central nervous system. However, the synthesis of new drugs to inhibit Cannabinoid type 1 receptors has not escaped the interest of researchers. In 2010, OOO Company, “NPF”, “Materials Medical Holding” registered a relatively mild drug called Dietress. However, it did not take long for this drug to be as successful as the others.

Although the failure of physicians to treat morbid obesity conservatively led to the abandonment of pharmacological drugs, individual researchers continued to search for new pharmacological drugs. At this stage, the search for drugs is aimed at creating a feeling of satiety. For this purpose, Gelesis Inc. Company has produced the drug in tablet form. This drug dissolves in the stomach and prevents the intake of excess food by creating a feeling of satiety (Nerobeev, 2014).

Thus, many drugs corresponding to the pathophysiological mechanism of morbid obesity and developed from it of non-alcoholic liver obesity (pentoxifylline, rosiglitazone, orlistat pioglitazone, metformin glucagon-like peptide 1 (GLP-1), vitamin E, angiotensin receptor blockers, probiotics, synobiotics) was synthesized and widely used in medical practice. The drugs synthesized should reduce insulin resistance, eliminate inflammation and, most importantly, reduce body weight.

One of such drugs is Orlistat, synthesized in 1998 in Belarus by Lekfarma Production Association. The proponent of this drug, S.A.Harriston and colleagues (2009) claim that patients with morbid obesity, as well as non-alcoholic hepatic obesity, had positive results from Orlistat by activating physical activity. According to the author, this drug, along with increasing physical activity significantly reduces body weight and improves the functional state of the liver.

We consider unfounded the arguments for the positive effect of the Orlistat given by S.A.Harriston and his colleagues in the article "Orlistat for patients with overweight and non-alcoholic steatohepatitis: randomized prospective study" published in 2009. First, the research was not divided into groups. As a rule, only Orlistat should be given to 1 group of patients. Without conducting such a study, it is incorrect for the authors to explain the positive result obtained under the influence of Orlistat. This is because by increasing physical activity during the day, for example, walking at a distance of 5-10 km at a brisk pace can lower body weight even without taking medication.

Clarification of the mechanism of pharmacological action of the drug is also not in its favor.

H.K.Lee has shown that this drug absorbs into the stomach and blocks the lipase molecule, which in turn prevents enzymes from breaking down fat (Lee et al., 2009). For this reason, about 30% of triglycerides are not absorbed by the body.

On the other hand, Riyan et al. (Ryan et al., 2010), James et al. (James et al., 2010) and others note that Orlistat is a contraindication for diseases of the cardiovascular system. In this regard, the use of Orlistat in morbid obesity is not recommended. Because, morbid obesity is the most associated disease of the cardiovascular system.

C.Zein et al. noted that pentoxifylline not only reduces body weight to some extent, but also has an emollient effect on non-alcoholic steatohepatitis (Zein et al., 2011). However, the results obtained cannot be considered reliable, as the drug was administered to 9 patients. On the other hand, the authors did not provide information in the article about the long-term consequences of taking the drug.

V.Ratziu et al. have found that rosliglitazone improves steatohepatosis level and significantly lowers aminotransferase level in blood (Ratziu et al., 2008). It is known that aminotransferase is a marker that reflects the functional state of the liver. In this regard, rosliglitazone can be considered a useful drug for the treatment of non-alcoholic steatohepatosis of the liver. However, Yu. Takahashi and colleagues have shown that rosliglitazone is a high risk factor for coronary heart disease (Takahashi et al., 2015). Taking into account that high body weight is a factor that accelerates atherosclerosis and creates real conditions for ischemia of the heart, it can be assumed that the use of rosliglitazone has a greater risk of developing myocardial pathology than the therapeutic effect.

In addition, the sale of this drug is currently completely banned in Europe, although it is partially banned in the United States.

Pioglitazone has been shown to significantly reduce elevated aminotransferase concentrations in the blood. Signs of steatosis and inflammation in the liver samples of these individuals showed a significant change in the positive direction (Sanyal et al., 2010).

However, pioglitazone is also banned in European countries because it is a trigger for bladder cancer.

Positive histological changes in the structure of the liver also occur after the administration of Liraglutide, a glycogen-like peptide-1 (GLP-1) analogue (Armstrong et al., 2016). However, although this study was a randomized study, no long-term results of the drug have been reported. The authors described only 48 hours of changes. In our opinion, the fact that the histological profile of the liver changes in a positive direction within 48 hours of any drug is not very convincing.

There are also various reports in the scientific literature on the consequences of taking Vitamin E in patients with non-alcoholic hepatic steatohepatosis with diabetes mellitus (Sanyal et al., 2010).

These data suggest that Vitamin E may have a positive effect on steatosis due to its antioxidant properties. However, numerous studies (Yoneda et al., 2010; Klein et al., 2011; Takeshita et al., 2014) have unequivocally shown that long-term intake of Vitamin E increases the risk of prostate cancer. Therefore, we believe that the use of Vitamin E in non-alcoholic steatohepatosis of the liver is unacceptable.

Sibturamine has also been widely used in the treatment of morbid obesity.

Sibturamine selectively captures serotonin and norepinephrine on the back side and stores them in brain neurons. This affects both parts of the energy balance. Therefore, unlike other drugs, sibturamine is a centrally acting drug that affects the donaminergic system (Florentin et al., 2008). In the Russian Federation, sibturamine is used under the name Reduksin. According to opinion of the researchers, sibturamine has a strong effect on 79% of patients, reducing their body weight and helping

to maintain that level for a long time (Vlasova et al., 2012; Romantsova et al., 2012; Ametov, 2013). At the same time, Sibutramine has attracted attention with its stimulating effect on carbohydrate metabolism, blood lipid profile and blood pressure.

An analysis of the literary data suggests that at morbid obesity lifestyle changes, increased physical activity, different diets, or medications does not provide a basis for complete cure of the disease. Summerbell et al. rightly point out that after stopping taking both drugs and drugs to reduce body weight, body weight begins to increase again (Summerbell et al., 2008).

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Morbid piylənmədə konservativ müalicənin rolu

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Məqalədə uzun bir dövr ərzində bədən kütləsinin artmasının, morbid piylənmənin və qaraciyərin qeyri-alkoqol mənşəli steatihepatozunun dərman, diyeta, həyat tərzinin dəyişdirilməsi, fiziki aktivlik vasitəsilə müalicəsi üsulları təhlil edilmişdir. Ədəbiyyat məlumatlarının təhlilindən belə bir qənaətə gəlinmişdir ki, morbid piylənmə zamanı istər həyat tərzinin dəyişdirilməsi, fiziki fəallığın artırılması, müxtəlif diyetalardan istifadə edilməsi və eləcədə dərman preparatlarının qəbulu xəstəliyin tam müalicəsinə zəmin yaratmır. İstər dərman preparatlarının və istərsə də bədən kütləsinin aşağı salınmasına yönəlmiş vasitələrin qəbulu dayandırıldıqdan sonra bədən kütləsi yenidən artmağa başlayır.

Açar sözlər: *Bədən kütləsi, morbid piylənmə, diyeta, dərman müalicəsi*

Роль консервативного лечения при патологическом ожирении

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В статье анализируются методы лечения в течение длительного периода увеличения веса, патологического ожирения и неалкогольного стеатогепатоза печени с помощью медикаментов, диеты, изменения образа жизни, физической активности. Анализ литературы показывает, что при патологическом ожирении изменение образа жизни, повышение физической активности, использование различных диет, а также лекарственных препаратов не обеспечивают полное излечение заболевания. После прекращения приема как лекарственных препаратов, так и средств для похудения, вес тела снова начинает расти.

Ключевые слова: *Масса тела, патологическое ожирение, диета, медикаментозное лечение*